Section 1: The Healthcare Continuum Model

The Healthcare Continuum Model (HCCM) is based on situational risk due to the specific task or setting, or due to underlying conditions, such as susceptibility of the host. Health hazards and exposure characteristics are the main parameters of the framework. The HCCM framework for topical antimicrobial products addresses the need to mitigate the risk of acquiring or transmitting organisms or disease in specific situations. The general population, food service and food preparation workers, and healthcare professionals use topical antimicrobial products in domestic, institutional, commercial, and healthcare settings. The risk of infection or acquisition of disease from the transmission of microorganisms can be correlated to specific tasks in all of these settings. The exposure, and consequently the risk, to populations of varying susceptibility determines the desired drug performance and the attributes necessary to mitigate the risk (e.g. fast-acting and persistent).

In September 1999, the Coalition submitted a briefing document to FDA proposing finished product efficacy testing of healthcare antiseptic drug products[3]. We concur with FDA on the approach of using both *in vitro* and *in vivo* efficacy testing. We recommended conducting Time Kill Tests (*in vitro*) to demonstrate the potential speed of antibacterial activity of a topical antimicrobial product. We also recommended conducting simulated use tests (*in vivo*) specific to the use scenario of the product.

In August 2001, the Coalition submitted a Citizen Petition that summarized the benefits of all topical antimicrobial products and suggested performance criteria using the appropriate *in vivo* simulated use test for three product categories: patient pre-operative preparation, surgical hand scrub, and healthcare personnel handwash. In this submission the Coalition proposes performance criteria using the appropriate *in vivo* simulated use test for three additional product categories: consumer body products, consumer hand products, and food handler preparations.

Situations Considered Herein

The home plays an important role in a number of public health and hygiene issues including the spread of foodborne infections and gastrointestinal infections, the common cold and other respiratory infections, and the development of skin infections (Scott *et al.* 2001, Kagan *et al.* 2002).

A number of surveys of bacterial contaminants of the home have been conducted. Moist areas of kitchens, bathrooms and fabrics (e.g. towels) are frequently found to be highly contaminated with potentially pathogenic organisms. The human body and its wastes are believed to be one of the major sources of these organisms. *Staphylococcus aureus* was isolated from 44% of hand towels and 20% of bathroom floors (Finch *et al.* 1978). *Escherichia coli* and other gram-negative bacteria were found to commonly contaminate wet areas such as sinks, drains, sponges, and dishcloths. They were also found, less frequently, on hard surfaces where there had been hand contact (Scott *et al.* 2001). Additionally, contaminated foods, *e.g.*, chicken carcasses, eggs, produce, serve as another source of pathogenic organisms in kitchens. The likelihood of the transfer of these organisms, either directly from one person to another or indirectly via inanimate objects or ingestion of contaminated foods, will depend upon the hygiene practices of the residents. The risk of infection will depend upon the exposure to the pathogen and the underlying health status of the person acquiring the pathogen.

Rubin (1988) estimated that when one person in a household becomes sick with a Salmonella infection, there is a 60% chance that at least one other family member will also become infected. These secondary infections are caused, in large part, by both direct and indirect cross-contamination in the home. It is likely that a similar pattern is true for other infections transmitted

[3] Additional data relating to finished product test methodology was submitted to the docket as a Citizen Petition on November 28, 2001.

by the fecal-oral route. Studies have shown that up to 50% of family members become infected when a child contracts *Shigella sonnei* dysentery. This is primarily a result of cross-contamination involving both the hands and inanimate surfaces (Thomas and Tillett 1973).

There is growing consensus among food experts that most cases of foodborne illness originate from food eaten in the home (Fein *et al.* 1995). In a US study of an *E. coli* 0157 outbreak, it was found that 80% of the likely source of contamination (hamburger) was eaten at home, and food preparers in those homes were significantly less likely to report washing their hands or work surfaces than were food preparers in the control households (Mead *et al.* 1997).

A number of studies have demonstrated the potential for hand transfer of either naturally occurring or seeded bacteria from contaminated food products (Humphrey *et al.*, 1994; Cogan *et al.* 1999). The potential for cross-contamination in the kitchen to cause foodborne illness was found to range as high as 39% (Djuretic *et al.* 1996, Evans *et al.* 1998).

The potential for the transmission of pathogens to oneself or to others in the home via direct or indirect means is significant. Topical antimicrobial products are used in domestic situations for both body and handwashing for the purpose of decreasing the overall bacterial load on the skin and thereby reducing the risk of transmission of disease to oneself or to another.

The reduction of the bacterial load on the skin is also important in reducing the transmission of disease to oneself or others outside the home. Topical antimicrobial products are used in many situations outside the home. Examples of institutional and commercial settings include, but are not limited to:

- public restrooms
- schools
- restaurants
- day-care centers
- long-term and residential care facilities
- prisons and correctional facilities
- manufacturing sites, e.g. pharmaceutical manufacturing
- food manufacturing and processing facilities
- offices of physicians, dentists, and other healthcare providers

In these cases, there is a need to reduce the numbers of bacteria and viruses that can be transferred to shared inanimate objects, food, or to other people. In many of these cases, a single source of infection can transfer that infection to many other people through direct or indirect contact. Reducing the bioburden on the skin has been shown to reduce the risk of disease transmission. (Black *et al.* 1981, McFarland *et al.* 1989, Boyce *et al.* 1994)

Exposure

Within the HCCM framework are two main levels of risk: risk of invasive exposure, i.e. the skin barrier is broken, and risk of disease transmission via non-invasive routes. Risk of non-invasive exposure is further sub-divided into risk of microbial transmission to others, either directly or indirectly, and risk to oneself *e.g.,* fecal-oral transmission.

i. Invasive

This submission will not discuss purposeful invasion of the skin integrity due to injections, surgery or catheterization[4]. However, invasive procedures that break the skin barrier are not restricted to a hospital environment. For instance, individuals in the home receiving home-dialysis, self-injecting drugs, or maintaining in-dwelling catheters are at serious risk of infection if hygienic conditions are not maintained. Topical antimicrobial products specifically designated for use in healthcare settings would be the preferred prophylactics in these situations. However, products designed for use by the general population could also be used, assuming they meet the appropriate criteria.

In the healthy general population, the risk of invasive exposure is usually limited to infection primarily by resident bacteria of overt cuts and scratches or microscopic openings in the skin caused by poor skin condition. The normal resident flora of the skin consists predominately of coagulase negative staphylococci, micrococci and coryneforms. Certain individuals are also carriers of *Staphylococcus aureus* and streptococci. In situations where the skin is stressed, these bacteria have been shown to cause overt disease *e.g.*, impetigo (Noble 1992), and/or to further aggravate skin conditions such as atopic dermatitis (Williams *et al.* 1990) or acne (Brown 1977). Topical antimicrobial products can be used to control the numbers and types of bacteria on the skin and can help to mitigate the risk of overt infection or the aggravation of skin conditions.

ii. Non-Invasive

There is a risk of transmission of microbial contaminants, primarily transient organisms, to oneself or from one person to another, either directly through hand-to-hand transmission or indirectly via transmission from food or other inanimate objects.

Transient organisms are those that may be found on the skin but do not normally colonize the skin; many are potential pathogens (Ayliffe 1980). The transfer of transient bacteria via hands is recognized as a common factor in the spread of disease (Maki 1978, Doebbling *et al.* 1992, Bryan *et al.* 1995, Boyle and Pittet 2002). The acquisition of illness may be associated with transmission of transient organisms on the skin to oneself via fecal-oral or respiratory routes. In addition, disease may be transmitted via the hands directly or indirectly to others, which may lead to food poisoning, other enteric diseases, and respiratory infections. An example of direct transmission is seen in daycare situations. Several studies of environmental surfaces in daycare settings have shown that fecal contamination is widespread. Approximately 30% and 20% of hands of children and adult caregivers, respectively, were shown to be contaminated (Ekanem *et al.* 1983, Weniger *et al.* 1983, Van *et al.* 1991). An example of indirect transmission involves currency. Studies of US currency found potential pathogens on 3-18% of the coins and 7-42% of the bills tested (Abrams and Waterman 1972, Jiang and Doyle 1999). These pathogens included *E. coli*, *Pseudomonas aeruginosa*, and *S. aureus*.

The total population is exposed daily to a variety of transient microorganisms depending upon the activities of the individual. The risk of developing an infectious disease depends on many factors, including the virulence and dose of the microorganism and the susceptibility of the host.

The primary means of interrupting the spread of infection are the application of sound principles of personal hygiene, disinfection of contaminated materials, and skin antisepsis. Risk management steps by the individual can interrupt transmission to oneself and to others as well as to inanimate objects that can become sources to others. (Marshall 1997; Krilove *et al.* 1996; Caturelli *et al.* 1996; Hammond *et al.* 2000; Isaacs *et al.* 1989; Isaacs *et al.* 1991).

[4] August 30, 2001 Citizen Petition addressed the use of topical antimicrobial products in these situations.

While plain soaps can remove pathogenic microorganisms from the skin, topical antimicrobial products can provide an incremental improvement in reducing the numbers of contaminants by either inhibiting or killing the microorganisms left on the skin in addition to removing microorganisms from the skin during the washing process (Montville *et al.* 2002, MacKenzie 1970, Keswick *et al.* 1997)

Summary

Control of microorganisms found on the skin of individuals is important to public health. The potential for the transmission of opportunistic pathogens to oneself or to others is significant, in the home, in institutional and commercial settings, as well as in healthcare settings. The risk of infection or acquisition of disease from the transmission of microorganisms can be correlated to specific tasks in all of these settings. The exposure and, consequently, the risk to populations of varying susceptibilities determine the drug performance desired and the attributes necessary to mitigate the risk.

Products such as consumer hand wash, consumer body wash and food handler products are intended to reduce resident and transient organism populations greater than can be achieved through the use of plain soap. This additional reduction translates to risk reduction in the transmission of potentially pathogenic organisms and in the potential for disease acquisition (Breneman *et al.* 1998, Rose and Haas 1999).